1961 ✓ (87)

R. W. SPERRY
California Institute of Technology

ORDERLY FUNCTION WITH DISORDERED STRUCTURE

I shall try to make my comments as brief as possible, for I suspect that anything that I can contribute here is likely to be toward the periphery of our symposium. I was under the misapprehension that a majority of the conferees would be engineers interested in devising ingenious circuits for servomechanisms and the like, who would have a timely concern for the problem of building compact control boxes that would continue to control after being nicked by a meteorite, peppered by radiation, or even pierced by a few bullets. With this in mind, I plan to start by recalling the always remarkable capacity of the cerebral machinery to continue to operate effectively and in relatively orderly manner in the face of extensive damage to the structure.

As most of you know, when large lesions are inflicted in the brain, or even a whole lobe removed, like the temporal or frontal, the cerebral machinery may continue to operate in such good fashion that most of us could not detect any functional change. It often requires very sensitive tests indeed to detect even major unilateral damage, while for some brain areas the tests have yet to be devised that will expose the defect.

Another point in regard to the preservation of function after large lesions is the fact that the nearby cortical networks generally continue to work effectively right to the very edge of the damaged tissue. For example, the outline of a blind spot in the visual field produced by a cortical lesion may be mapped by having the subject follow a moving object as it approaches from different directions to disappear into the blind area.

Remarkable preservation of function is seen also after diffuse damage like that found in approaching senility or after disease

where vast numbers of cells may be eliminated in scattered arrays all through the system. So long as a moderate percentage of the remaining neuronal elements survive and regain a healthy state, organized function is recovered.

In some of our laboratory work we have had occasion to riddle the visual and surrounding cortex of the cat with pins or needles of tantalum wire. Dozens of pins were poked into and through the cortical tissue in pin cushion fashion until the whole visual cortex was saturated and our patience exhausted. The biologically inert inserts were simply left in the brain. In subsequent testing of near-threshold pattern discrimination the visual performance was practically as good as before.

The ability of the cortex to function close to the edge of lesions is most strikingly illustrated perhaps in some experiments that involved multiple intersecting knife cuts. Cross-slicing of cortical areas with numerous criss-cross knife cuts extending vertically through the depth of the cortex and placed only a few millimetres apart was found to have very little effect on organized function in the scored area. Figure 1a shows the brain of a cat in which the visual cortex has been subdivided in this way. The animal appeared quite blind for the first four days after surgery, but as the post-operative edema began to clear, vision reappeared and continued to improve during the next month and a half until the animal's level of performance on pattern discrimination tests was within the normal range. This cat was able to pick out the equilateral triangle shown in the center of Figure 1b when it was paired with any one of the other triangles surrounding it, under conditions controlled for position, odor and other non-visual cues.

In contrast to this preservation of organized function in the living brain, recall what happens in most of our man-made circuits as the result of a single burnt-out tube, a single broken wire, a single short circuit and so on. With an eye to future design principles for incorporating built-in repair, compensating, corrective and other self-organizing devices, it might be apropos to point out some of the design features of the living brain that enable it to continue to function in the face of extensive structural damage.

Although a complete explanation is still far out of reach, of course, there are a few things one can say. In the first place, it probably is not any single construction principle that is responsible.

There would seem to be at least several now recognizable and probably many yet to be worked out. I will run over a few points that come quickly to mind in this connection without particular regard to their order or relative importance and I am sure that others here more directly concerned with these problems will be able to add to the list.

There is, for example, the simple factor of multiple connection. Each fiber of the central nervous system usually terminates not on one terminal connection or two, but on ten, or more typically, hundreds or even thousands of downstream elements. Similarly, each neural fiber picks up from tens or hundreds of terminals at the other end.

A second factor is that of the wide overlap in the connections of nearby elements. For any two fibers running side by side in a given nerve cable or tract, the overlap among their multiple hookups at each end may run roughly on the order of say 60 per cent or higher. With this extensive overlap it is evident that a sizeable number of elements may be damaged or eliminated from the complex and the loss remain unnoticed. In some parts of the central network, or in all parts in some species, the neural elements have regenerative capacity with the result that a break in the central circuit is promptly repaired. The new connections formed in the regenerative process are as orderly and neatly arranged as were the original, because the same orderly forces of growth persist in these adults and operate in regeneration. It is as if each neuronal element has a kind of built-in navigation plan or homing instinct of its own that enables it to recover its appropriate hookups.

This kind of thing is illustrated in the studies on optic nerve regeneration already referred to by Dr. McCulloch earlier in the conference. After the nerve has been completely cut and there has been a thorough scrambling of fibers in the nerve scar, a given fiber approaching the point within the brain where the optic tract divides into medial and lateral branches, will select the correct branch according to whether its locus of origin was in the dorsal or the ventral quadrant of the retina. The medial and lateral bundles skirt around the medial and lateral edges respectively of the optic lobe of the midbrain, giving off fibers along the way as they progress from anterior to posterior poles of the lobe. A given regenerating fiber after choosing the correct branch along

the periphery of the lobe, then chooses correctly the proper point at which to enter the lobe. Fibers from the central retina enter near the center of the lobe, those from the nasal retina enter at posterior levels, and those from the temporal retina at anterior levels.

Once inside of the optic lobe or tectum, the fibers run from the periphery toward the center in a superficial parallel layer. Again, they are faced with numerous alternative possibilities with regard to the point at which they will each leave the parallel layer to dip downward into the underlying plexiform layer. Fibers from the peripheral retina dip quickly near the periphery of the tectum. Those from the central retina remain in the parallel layer to cross the peripheral portions of the tectum and dip downward only after they reach the central tectum. In the plexiform layer each fiber branches and forms multiple contacts with the dendrites and cell bodies of the tectal neurons. Again, we must infer a selective choice in synaptic formation among the numerous possible alternatives. The latter inference is based largely on the fact that the trained discrimination of red, blue, yellow, green, gray and other colors from one another in a large variety of combinations has been shown to be restored in its original form after optic nerve regeneration.[1] (It is of further interest here that the newly regenerated pattern of central synapses is adequate for reactivation of the memory for visual discrimination habits learned with the original synaptic connections prior to optic nerve section. And incidentally, the restored color discrimination performance survives ablation of forebrain plus cerebellum.)

The foregoing description is based on studies in fishes. The central nervous system of the mammal, of course, is not capable of much functional regeneration. Even in the mammalian cortex, however, it is conceivable that the detailed pattern of synaptic connections is in a state of continuous flux and that the normal pattern is prevented from drifting into a state of randomized chaos by the constant operation of specific biochemical forces within the individual elements similar to those responsible for orderly central regeneration in the lower vertebrates.

A fourth factor tending to preserve organized activity may be described as the multiple reinforcement of any given function from numerous different sources, any one of which may in itself

be capable of sustaining the activity. As a simple example, take a locomotor gait, such as the running, trotting, or galloping of a horse or dog. It appears that the feedback of any single one of the four limbs in action is sufficient to keep the whole system running. In fact, experiments dealing with the control of the locomotor gait in amphibians show that the sensory nerves of the entire spinal system may be eliminated except for those in just one or two of the dorsal roots and these will be sufficient to keep the locomotor gait going.[5] Furthermore, it does not matter which two are left; any two will do. Thus, in the normal condition there is an extensive multiple reinforcement of the same pattern from many different sources. Presumably a given cerebral pattern may also be activated and sustained by numerous "mental associations". Redundancy is one element here, perhaps, but this kind of multiple reinforcement involves, of course, a good deal more than simple redundancy.

Part of the problem of maintaining organized activity lies in controlling and preventing disrupting and disturbing influences from other unrelated functions. In this respect functional control factors like "reciprocal inhibition" and "inhibitory surround" must play important roles.

Another point, a bit less relevant perhaps but the very essence of self-organization, is that the guidance and control of sequential activity in the nervous system in general does not depend upon a central schedule or clock for ticking off each act at its proper time—excepting perhaps in the case of very simple cycles or for extremely rapid sequences like consecutive finger movements in piano playing. The much more general method of cerebral control is to have each act set off and sustained only by those conditions for which the act is appropriate and which usually are a product of the preceding act in the sequence. In this way the sequence runs itself. Further, with this type of control many kinds of disturbances and changes in speed and timing and the like may occur without disrupting the whole pattern.

The circuitry by which all this is achieved may be likened to a vast collection of negative feedback systems, multiply interlocked with one another and broadly organized throughout on a hierarchical plan, that is, a tremendous network of interlocked checks and balances permeated by homeostatic loops within loops.

A minor safety factor may be seen in the arrangement of the cortical circuits along vertical rather than horizontal dimensions. This accounts in part for the ability of small portions of cross-cut areas and/or remnants adjacent to large lesions to continue their orderly function.

Another simple and obvious safety factor is that of right–left duplication. Brain centers, much like kidneys, lungs, gonads and other organs, are furnished in matched pairs. Damage to or complete loss of one member often is not critical because the function involved can be handled by the other member on the opposite side. This would seem to apply to the frontal and temporal lobes of most mammals and to many of the hypothalamic and other homeostatic control centers.

Studies involving hemispherectomy and commissurotomy suggest that the mammalian brain is in many ways essentially two separate half-brains, that is, two whole control systems, each capable of carrying on independently of the other. Similarly, the chances that a black control box sent into space will be put out of commission by a shell, may be reduced by half if it has two independent and separated control circuits properly oriented.

This raises another problem in the circuitry of higher controls. If one has two complete sets of higher level controls, is there any advantage to building cross connections between these? The answer would seem definitely to be "yes" if the example of the mammalian brain means anything. In the mammalian brain the largest single fiber tract by far is the corpus callosum—the system of fibers that interconnects the neocortex of the two cerebral hemispheres.

Which brings us to the "riddle of the corpus callosum", certain aspects of which have definite relevance to our topic of self-organization. First perhaps it should be pointed out that it is no longer the enigmatic riddle that it was a little over ten years ago when Dr. McCulloch somewhat facetiously but not without good justification stated that the only known function of this structure was to aid in the transmission of epileptic seizures from one side of the body to the other. About the same time Lashley, in a similar vein, used to suggest that the only apparent function for the corpus callosum seemed to be mainly mechanical in nature, i.e. to prevent the two hemispheres from sagging too far apart.

Today it is probably fair to say that more is known about the anatomy and the physiology of this particular cortico-cortical fiber system than about any other in the brain. Embedded deeply at each end in the cortical networks, any information about its connection plan and function is bound to have implications for the secrets of cortical organization in general. Most of this new information regarding the function of the corpus callosum and other cerebral commissures has been obtained from animal studies of the past six or seven years, which I will not attempt to go into in any detail here since they have only recently been reviewed elsewhere.[3,4,6]

For our present purposes it will be enough to point out that in the absence of the cerebral commissure, i.e. following their surgical section in the midline, a cat or monkey is in many respects like an animal with two brains in the place of one. Having two instead of one brain seems to make little difference under most ordinary conditions. In fact, the cat or monkey even after deep bisection of the brain through the quadrigeminal plate and the cerebellum is hardly distinguishable from its normal cagemates under ordinary circumstances. With the proper testing conditions, however, wherein one can stimulate and train each hemisphere independently, it is possible to show that in the absence of the cerebral commissures each hemisphere has its own perceptual, learning and memory processes, i.e. its own cognitive or psychic system. It is as if neither of the separated hemispheres has any longer any direct awareness of the mental activity of the other, nor any direct memory of anything experienced by the other subsequent to section of the commissure. The control of the animal's behavior under these conditions may be governed predominantly from one of its half brains if one hemisphere is markedly dominant, or the control may shift from one to the other and back in an alternate fugue-like fashion, or the two hemispheres may continue to operate simultaneously in parallel so long as their lower level effects are harmonious. With proper testing conditions it can be shown that the two half brains can operate simultaneously in the learning of separate—even conflicting—discrimination habits.

There are some advantages perhaps in having the two cerebral control systems working independently, but presumably these are

outweighed by the disadvantages. In the separated condition neither hemisphere benefits from the learning and experience of the other. In a sense, the commissures thus serve to keep each hemisphere up to date on what is new in the other. They appear also to facilitate certain sensory–sensory and sensory–motor integrations—as for example volitional visual uses of the hand across the midline of the visual field.

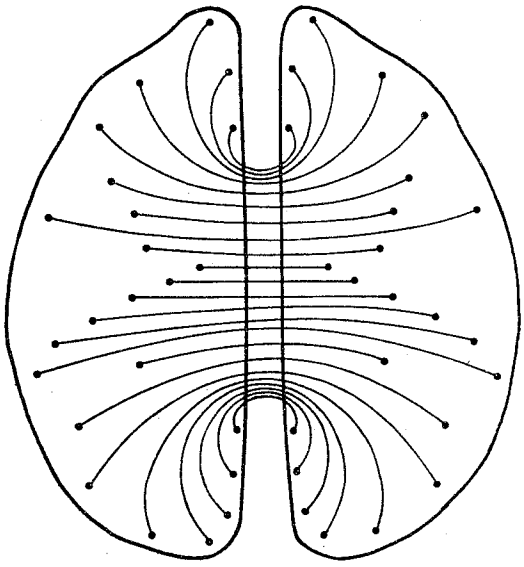

FIG. 2. Homotopic principle of callosal cross-connections between corresponding loci of right and left hemisphere.

There is still one aspect of the corpus callosum that remains something of a real riddle: namely, the problem of the meaning of the bilateral symmetry of its cross connections. Physiological and anatomical studies indicate that the great majority (though not all) of the fibers of the callosum are homotopic, that is, the fibers arising from a given point in one hemisphere project across the midline to the same point in the opposite hemisphere.(4) This homotopic principle is illustrated in Figure 2. More than this, it seems that within these symmetrical loci the fiber systems arising

from different layers of the cortex tend to terminate predominantly in the same layer on the opposite side.[6]

The question, then, is this: "What good, from an engineering standpoint, is served by having this tremendous system of fiber interconnections linking identical points in the two hemispheres?" It would appear that any activity pattern in one cerebral cortex

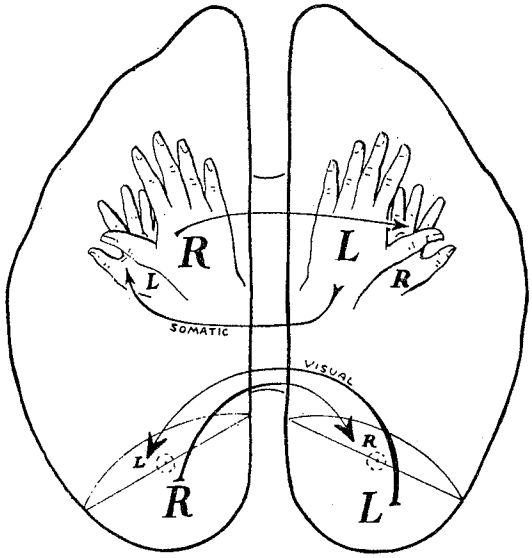

FIG. 3. Hypothetical alternative to homotopic cross-connections, the principle of "supplemental complementarity".

would tend to be duplicated by the corpus callosum in the other—that the corpus callosum would thus act as a symmetrizing influence on all cerebral activity.

What good would it do to have cross connections between the representations of identical points in right and left halves of the visual fields? The same can be asked with respect to corresponding points on right and left sides of the body. Except in rare instances when the two halves of the visual field or the body contacts on right and left sides are mirror images, it would seem that such interaction could only make for confusion.

Instead of symmetric cross connections it would seem to make

more sense offhand to have the cross connections more supplemental or complementary in nature as suggested in Fig. 3. This figure illustrates an older notion I had about the corpus callosum that has been reactivated by this conference. This plan is quite speculative with little evidence to support it. Instead of having the right half of the visual field reciprocally cross connected to the left half, in this scheme each half is cross projected so as to supplement the direct projection. This gives in each hemisphere a whole visual field—or its representation in a subsequent step of the data processing system. The same applies to the representation of the body surface and other sensory fields, and also to deeper association activities of the hemisphere. In an effort to keep up with our modern physicists, I used to call this the "principle of supplemental complementarity".

Actually the evidence is not yet sufficient to completely rule out some scheme of this kind. There is something puzzling and irregular about the callosal cross connections between the visual areas of the cortex. In the cortical map of the body surface, the contralateral and ipsilateral representations seem to be in register so that a supplemental scheme would be difficult to differentiate from one of symmetrical reciprocity. In the past investigators of the callosum were not searching with such questions in mind, but the time is now ripe for more detailed investigations of the meaning of the cross connection pattern. It is accepted that a minority of the callosal connections are heterotopic in nature and in some instances the fibers from a cortical area project to quite different regions on the other side.

Possibly both symmetric and supplemental as well as other schemes are represented in the corpus callosum. Perhaps the symmetric system serves as a great detector of all-important asymmetry. In any case, you see the problem. It is a circuitry problem essentially, and the kind of thing that may well be answered more quickly in the developing logics of artificial intelligence than in the probing of the neurophysiologist.

REFERENCES

1. H. L. ARORA and R. W. SPERRY, Studies on color discrimination following optic nerve regeneration in the cichlid fish, *Astranotus ocellatus*, *Anat. Rec.* **131**, p. 529 (1958).

2. D. ATTARDI and R. W. SPERRY, Central routes taken by regenerating optic fibers, *The Physiologist* **3**, p. 12 (1960).
3. F. BREMER, J. BRIHAYE and G. ANDRE-BALISAUX, Physiologie et pathologie du corps calleux, *Arch. Suisses Neurol. Psychiat.* **78**, p. 31 (1956).
4. B. Grafstein, Organization of callosal connections in suprasylvian gyrus of cat, *J. Neurophysiol.* **22**, pp. 504–15 (1959).
5. J. GRAY and H. W. LISSMAN, Further observations on the effect of deafferentation on the locomotory activity of amphibian limbs, *J. exp. Biol.* **23**, pp. 121–32 (1946).
6. R. E. MYERS, Interhemispheric interconnections between occipital poles of the monkey brain, *Anat. Rec.* **136**, p. 249 (1960).
7. R. W. SPERRY, Some developments in brain lesion studies of learning, *Fed. Proc.* (in press).
8. R. W. SPERRY, Cerebral organization and behavior, *Science* **133**, p. 1749 (1961).

DISCUSSION

DR. YOVITS: What happens when the individual cortical halves give completely opposite orders to the animal body? Does the animal eventually learn to disregard one order?

DR. SPERRY: Yes, in general one or the other hemisphere tends to dominate the lower centers and motor outflow and these consistently follow the dictates of the dominant control. Any incompatible orders coming down from the other hemisphere tend to be ignored or inhibited. It is one of the important features of brain organization that it does not get confused. It is a this-or-that proposition: either this or that but never "thiast" or other mixtures. There are exceptions, but they are the exceptions that prove the rule. There is some built-in mechanism including perhaps "reciprocal innervation" and "inhibitory surround" as mentioned above, that makes for unified activity. Once an activity pattern gains the ascendancy it wipes out thousands of other possibilities. If you can build that into a machine you can perhaps begin to get some of the "many-machines-in-one" kind of versatility we see in the brain.

DR. SHERWOOD: I think the point should be made here which arises from the surgical operations or experiments in man which someone in England has carried out. He has done a series of hemispherectomies for birth brain damage to children who keep having seizures in one hemisphere. Now the point that arises from this is that while the whole hemisphere is ablated with the exception of the basal ganglia—they are left—now, I have seen some of these children and their two-point discrimination on the decentralized side improves after hemispherectomy, as does their gait. It shows, I think, that the damage of a machine that works wrong, is worse than not having the machine.

CHAIRMAN BOWMAN: Is there any further discussion of Dr. Sperry's paper?

DR. MCCULLOCH: Yes, please. My statement concerning the corpus callosum was not made lightly. I have worked from, oh, the early thirties to the mid-forties on the anatomy and physiologically detectable anatomy of the system and at that time there were a large number of men who had had the corpus callosum, and the anterior commissures in some cases, cut in order to prevent spread of seizures from one hemisphere to the other, and if they cut the anterior commissure as well as the corpus callosum, they generally stopped having seizures that passed all the way over. There were some exceptions. Now the most interesting thing about the corpus callosum, to my

mind, is not this homeo-projection. It is that there exists, let's say, from area 8, from area 6, and from some parts of the post-central cortex, much more widely distributed afferents to the opposite hemisphere. There are more of these heterotopic fibers from areas that are farther removed from direct sensory and direct motor projections, and I think this is probably what you are looking for. My feeling is that it is more sensibly organized. The other thing is also not quite a frivolous remark. When you cut the two hemispheres, you form a caricature of the Post logic. So long as the two are coupled, point for point, you may remove, you may simplify the logial structure of the machine. That is the very fact that you have made symmetrical Venn's out of them, in miniature sections, that is clear. You have got a Post logic.

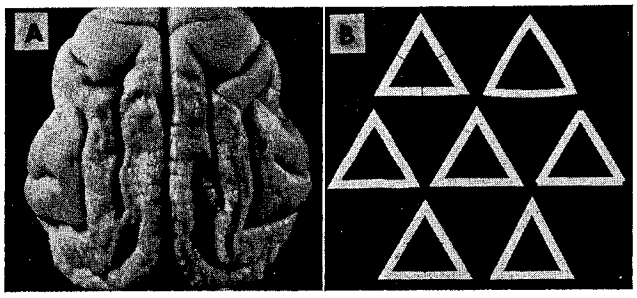

FIG. 1

[*facing page 280*